JACC Vol. 5, No. 6
June 1985:55B–56B



# Basic Principles of Electrophysiology: Summary

*Moderator:* **Borys Surawicz, MD, FACC;** *Panelists:* **Harry A. Fozzard, MD, FACC, Lawrence E. Hinkle, Jr., MD, Mario Vassalle, MD**

## Conclusions and Discussion

### *Dr. Surawicz's Conclusions*

In recent years, our understanding of the mechanisms of the initiation of ventricular fibrillation has increased because of a more precise mapping of the sequence of activation, both in experimental animal preparations and in human subjects. The discovery of the slow channel has improved our understanding of slow conduction, which is an essential ingredient of reentry. It appears that slow conduction in the process of microreentry may be caused by either slow channel-dependent "slow responses" or depressed "fast responses" in depolarized myocardium.

Determination of the ventricular fibrillation threshold continues to be used as a measure of vulnerability, but several theoretical and practical limitations of this technique have been elicited. It has been established that the ventricular fibrillation threshold is lowered in patients with coronary artery disease and inducible ventricular tachycardias. The R on T phenomenon plays a role in the primary ventricular fibrillation during acute myocardial ischemia, but not in the initiation of arrhythmias during other stages of ischemic heart disease. The use of ion-selective extracellular electrodes elucidated some of the biochemical derangements present during acute myocardial ischemia.

The electrical nonhomogeneity responsible for arrhythmias during ischemia is attributed predominantly to combined effects of $K^+$ and norepinephrine released from the ischemic myocardium. The role of acidosis and various metabolites in the genesis of ventricular fibrillation is less well established. The mechanism of ventricular fibrillation during coronary reperfusion appears to differ from that during occlusion. The congenital long QT interval is a model of an apparent neurogenic disorder of the heart precipitating or facilitating arrhythmias through increased dispersion of repolarization. In other situations, the significance of the prolonged QT interval is less certain because it is not known whether it represents a predictable manifestation of increased dispersion of repolarization, or whether an increased dispersion of repolarization constitutes an independent risk factor for arrhythmias and cardiac death in patients with coronary artery disease, cardiomyopathy, mitral valve prolapse and other forms of heart disease.

The inability to predict when prolongation of the QT interval is beneficial and when it is potentially harmful exemplifies an important deficiency in our knowledge concerning the role of dispersion of repolarization in arrhythmogenesis and in the pharmacologic treatment of ventricular arrhythmias.

### *Dr. Fozzard's Conclusions*

Electromechanical dissociation can be documented as a cause of death in some patients with acute cardiac ischemia. It is characterized by a normal electrical pattern (normal sinus rhythm) in the presence of the loss of contractile function of the left ventricle. It appears to be a small but significant cause of sudden cardiac death. Several clinical syndromes, including massive pulmonary embolism and cardiac rupture, can mimic this electromechanical dissociation so that its incidence is impossible to estimate accurately.

Experimental studies show that early ischemic contractile failure is associated with an intracellular acidosis, reducing the binding of $Ca^{2+}$ to troponin C. The acidosis is a consequence of continued anaerobic glycolysis and consequent lactic acid production. During this early period, the ability of the cell to store and release $Ca^{2+}$ in response to the electrical signal is nearly normal so that treatment with $Ca^{2+}$ or the positive inotropic drugs that act by increasing $Ca^{2+}$ is not beneficial. Other factors influencing the onset of contractile failure cannot yet be excluded because measurements of intracellular pH have not been made early enough to permit a direct correlation to be made. The role of the autonomic nervous system in triggering the sequence of events leading to electromechanical dissociation is also unclear and is a promising area for further study.

### *Dr. Vassalle's Conclusions*

Ventricular standstill can be caused by a variety of clinical conditions that depress the dominant and the subsidiary pacemakers. Profound differences exist between the sinus node and the idioventricular pacemakers. The sinus node is

Address for reprints: Borys Surawicz, MD, Krannert Institute of Cardiology, Indiana University School of Medicine, Department of Medicine, 1100 West Michigan Street, Indianapolis, Indiana 46223.



0735-1097/85/$3.30

JACC Vol. 5, No. 6
June 1985:55B–56B

functionally more versatile since it can use both sodium and calcium for activation, is more resilient because it is not affected by a block of the fast sodium channel, has a rate range that assures adequate responses, is not usually overdrive-suppressed, is not sensitive to high $(K)_o$ and is accelerated by high $(Ca)_o$. The Purkinje fibers can be activated only through the fast channel and are therefore susceptible to depression by local anesthetic agents and other antiarrhythmic substances, have a rate range that is barely sufficient to maintain cardiac output, are usually overdrive-suppressed, are sensitive to high $(K)_o$ and are slowed by high $(Ca)_o$. These differences reflect major differences in function: pacemaking for the sinus node and fast conduction of impulses for Purkinje fibers. The Purkinje fibers can become automatic under abnormal conditions (complete atrioventricular [AV] block), but their pacemaker activity is vulnerable to those influences that usually keep it in check. Accordingly, the Purkinje fibers may discharge too slowly to maintain an adequate cardiac output or may fail to discharge altogether if the regulatory factors (for example, ionic concentrations, overdrive suppression, temperature and sympathetic discharge) depart from the normal. The necessity of keeping the Purkinje fibers' automaticity in abeyance under normal circumstances is the factor that makes this tissue more likely to fail in its subsidiary function under abnormal circumstances.

In the presence of sinus rhythm idioventricular automaticity is not brought into play. However, the situation changes substantially when atrial pacemaker activity is suppressed or AV conduction is interrupted. In normal individuals, the subsiding of the overdrive suppression during ventricular standstill allows the establishment of a regular idioventricular rhythm after a few seconds. However, in certain patients, the depressed idioventricular automaticity and the consequent exaggeration of overdrive suppression will result in a prolonged ventricular arrest. Although the mechanism by which the pacemaker activity is depressed may vary (that is, structural damage, depression by electrolytes, drugs, anoxia and anesthetic agents), the result is the same, namely, a reduced ability to initiate a rhythmic ventricular discharge. This becomes most obvious when the sudden cessation of activation of the ventricles by the pacemakers allows the effects of overdrive suppression and depressed automaticity to become manifest.

## *Excerpts from Discussion*

*Question from Dr. Hinkle:* Is the long QT interval an indicator of increased dispersion of repolarization?

*Dr. Surawicz:* Not always. If the repolarization is uniformly prolonged, for example, during hypocalcemia or steady state hypothermia, the QT interval is prolonged but the dispersion is probably not increased. An indicator of increased dispersion of ventricular repolarization in human beings is the R on T phenomenon in the presence of a long QT interval. In this setting, the long QT interval signifies a long duration of repolarization in some region of the ventricle, and the short coupling interval (R on T) signifies a short duration of repolarization, that is, early recovery in some other region of the ventricle. Thus, the interval from the onset of a premature ventricular complex to the end of the T wave equals the minimal dispersion of repolarization.

*Question from the audience:* How important is the dispersion of repolarization in the genesis of arrhythmias?

*Dr. Surawicz:* This appears to vary in different types. For instance, in the congenital long QT syndrome, available evidence suggests that the dispersion of ventricular repolarization plays a critical role in genesis of the arrhythmia. However, in the experimental arrhythmia model of coronary reperfusion, dispersion of repolarization appears to play no more than a subordinate role. In other types of arrhythmia, the role of dispersion remains to be evaluated.